UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/828,068	04/06/2001	Yong-Hwan Moon	18941001400	7267

20350 7590 01/15/2003

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
BAUM, STUART F	
ART UNIT	**PAPER NUMBER**
1638	13

DATE MAILED: 01/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/828,068	MOON ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *6,11 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-5,7-10,12-16 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-20 are pending.

Applicant's election with traverse of Group I, claims 1-5, 7-10, 12-16 and 18-20 including SEQ ID NO:1 encoding SEQ ID NO:2 in Paper No. 12 is acknowledged. The traversal is on the ground(s) that Applicant believes an "undue burden" has not been established for searching both Groups I and II. Applicant contends that there would not be any difference in the search strategy between searching sense and antisense orientation of the claimed nucleic acid sequence. Applicant asserts that sense and antisense suppression of gene expression utilize the same mechanism. Lastly, Applicants note that in a related application (09/415,946, now U.S. Patent No. 6,376,751) sense and antisense constructs were examined together. This is not found persuasive because sense and antisense constructs have inherently different functions. Nucleic acid sequences oriented in sense orientation are used to increase the activity of an encoded polypeptide whereas nucleic acid sequences oriented in antisense orientation are inherently used to reduce the acitivity of an encoded polypeptide. Each orientation utilizes a different molecular mechanism and has a different outcome, product or phenotype. In the present application, Applicant did not specify in the claims that the sense oriented constructs were to be used to inhibit the acitivity of the encoded polypeptide and as such were treated as being used to increase the activity of the encoded polypeptide. In addition, while the search of the prior art for one group may overlap with that of another, they are not co-extensive of each other and thus would be a burden on the Office. Lastly, each application is examined on its own merits and the most recent PTO rules and regulations.

The requirement is still deemed proper and is therefore made FINAL.

Claims 6, 11, and 17 are withdrawn from consideration as being drawn to non-elected material.

Claims 1-5, 7-10, 12-16 and 18-20 are examined in the present Office Action.

Specification

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete any embedded hyperlink and/or other form of browser-executable code, see page 23, line 14 for example. See MPEP § 608.01.

Drawings

3. The drawings are objected to for the reasons indicated on the enclosed form PTO-948. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-5, 7-10, 12-16, and 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the metes and bounds of "an OsEMF1 polynucleotide" cannot be determined because it is unclear whether the polynucleotide is obtained from the activity of an OsEMF1

polypeptide or if there is a function associated with OsEMF1 polynucleotides which has not been explicitly described. All subsequent recitations of "an OsEMF1 polynucleotide" are also rejected.

In claim 1, second line, the word "which" should be changed to "wherein the".

In claim 1, the metes and bounds of "stringent conditions" have not been defined. Applicant has not explicitly stated in the specification the conditions and reagents associated with the claimed "hybridization conditions".

In claim 2, the metes and bounds of "at least about" have not been defined. The term "at least" specifies the lowest acceptable number whereas "about" denotes an approximation of some number.

In claim 7, second line, the word "which" should be changed to "wherein the".

In claim 8, "a heterologous" should be changed to "the heterologous".

In claim 13, the word "gene" should be omitted as SEQ ID NO:1 is not a "gene". This claim depends from claim 12, which describes a promoter. Does the promoter have to be a region of SEQ ID NO:1?

In claim 14, the term "modulating" is unclear. Applicant needs to explicitly state how the reproductive development has been changed.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: and wherein the introduced DNA is expressed in the transformed plant to affect reproductive development.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-5, 7-10, 12-16, and 18-20 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well established utility.

The claims are drawn to an isolated nucleic acid molecule that hybridizes to SEQ ID NO:1, a sequence that hybridizes to SEQ ID NO:1 and is at least 100 nucleotides in length, or a nucleic acid sequence of SEQ ID NO:1 encoding SEQ ID NO:2, a transgenic plant and a method of modulating reproductive development in a plant, both of which comprising transforming a plant with an isolated nucleic acid molecule that hybridizes to SEQ ID NO:1 and is operably linked to a plant promoter.

Applicants isolated the rice EMBRYONIC FLOWER (EMF1) homolog, OsEMF1, from rice using the rapid amplification of cDNA ends (RACE) technique. Applicants do not disclose any of the conditions, nor primers that were used to amplify the corresponding cDNA. Applicants have disclosed that the percent sequence identity between EMF1 and OsEMF1 is 20% (page 24, paragraph beginning on line 14), but Applicants have not disclosed the regions that are conserved between the two sequences nor have they disclosed if OsEMF1 has the same function as EMF1. Applicants only report that EMF and OsEMF1 do not display significant homology to proteins of known function (page 24, lines 26-27) and that a region of EMF shares 23% identity with two members of a nuclear receptor gene family (page 24, paragraph beginning on line 26) but they do not specify if OsEMF1 also contains this region. It is unclear if OsEMF1

has any function at all because Applicants have not transformed a plant with the nucleic acid encoding an OsEMF1 protein nor have they disclosed a rice plant with a mutant OsEMF1 gene. Based upon Applicant's disclosure, there is no clear nexus between their invention of SEQ ID NO:1 and any utility set forth to allow one skilled in the art at the time the invention was made to take the claimed invention and clearly and immediately achieve the benefits set forth.

In the instant application, Applicants have not disclosed if OsEMF1 contains all the domains necessary to produce a protein with the same activity as EMF1. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by Burgess et al (1990, J. Cell Biol. 111:2129-2138), who teach that the replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein.

The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252), who teach that a replacement of aspartic acid at position 47 with alanine or asparagine in transforming growth factor alpha had no effect, but that replacement with serine or glutamic acid sharply reduced biological activity (see the abstract). Small changes in amino acid sequence can completely modify enzymatic function; Broun et al (1998, Science 282:1315-1317) teach that a change of four amino acids converts an oleate 12-desaturase to a hydroxylase. McConnell et al (2001, Nature 411 (6838):709-713), teach that the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain. This change renders the protein constitutively active and therefore creates a dominant mutation which has a drastic alteration in phenotype compared to wild-type *Arabidopsis* plants. Thus, Lazar et al, Broun et al and McConnell demonstrated that one or few amino acid substitutions could dramatically affect the biological activity and the structure-function characteristics of a protein.

Even within a gene family, protein function is not conserved. Zhao et al (2001, Science 291 :306-309) teach that not all YUCCA-like genes have identical effects when overexpressed in plants. BAS3 which is a member of the YUCCA gene family and has 50% and 63% amino acid identity with YUCCA and YUCCA3, respectively produces plants with long hypocotyls when overexpressed in plants. This phenotype is in contrast to YUCCA, which produces plants with short hypocotyls when overexpressed as a dominant mutant (page 308, left column, 1st paragraph). Therefore, given the low sequence identity between OsEMF1 and EMF1 (20%,

page 24, paragraph that begins on line 14), additional work is required to verify the function of OsEMF1.

While Applicant is not required to provide empirical data to verify that OsEMF1 of SEQ ID NO:1 has the same activity as EMF1, a functional assignment based upon sequence alignment should be a starting point for determining a particular activity of a protein, and should not replace empirical verification of a tentative functional assignment. In regards to Applicant's SEQ ID NO:1, how and under what conditions should a nucleic acid encoding SEQ ID NO:2 be used to alter flowering time. For example, in which tissues does it need to be expressed to achieve the purported advantage. It is apparent that extensive further research, not considered to be routine experimentation, would be required before one skilled in the art would know how to use the claimed invention. It has been established in the courts that a utility which requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use is not a substantial utility:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an application to engross what may prove to be a broad field." (*Brenner v. Manson,* 383 U.S. 519 (1966)).

Thus, while a developmental process such as altering flowering time would provide substantial benefit to the public, it is unclear how one of ordinary skill in the art would be able to utilize Applicant's nucleic acid of SEQ ID NO:1 encoding SEQ ID NO:2 to alter flowering time without having to carry out further research. Accordingly, the claimed invention lacks a "credible real-world" use.

In addressing claims drawn to sequences that hybridize to SEQ ID NO:1 or sequences that hybridize to SEQ ID NO:1 and are at least 100 nucleotides in length, since SEQ ID NO:1 lacks utility for the reasons set forth above, sequences having less than 100% sequence identity to SEQ ID NO:1 would also lack utility. Again, Applicant should note that no region of the protein encoded by SEQ ID NO:1 has been identified to be essential for its proper acitivy. Also, no working examples of any sequence are set forth in Applicant's disclosure.

Additionally, there also is no well-established utility for SEQ ID NO:1. SEQ ID NO:1 does not have a well-established utility for hybridization purposes because the encoded protein does not have utility for the reasons indicated above. Accordingly, the claimed invention lack utility.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-5, 7-10, 12-16, and 18-20 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Written Description

7. Claims 1-2, 4-5, 8-9, 12-15, and 19-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated nucleic acid molecule that hybridizes to SEQ ID NO:1, a transgenic plant comprising said nucleic acid molecule, a method of modulating reproductive development in a plant comprising a heterologous OsEMF1 polynucleotide, and an isolated nucleic acid molecule that hybridizes to SEQ ID NO:1 and is at least 100 nucleotides in length. The specification only discloses the nucleic acid sequence of SEQ ID NO:1 encoding SEQ ID NO:2 and does not disclose all the sequences that would hybridize to SEQ ID NO:1 even under any hybridization conditions. Applicant has not disclosed any specific structural, physical and/or chemical properties for the claimed sequence nor does Applicant describe the structural features specific for any heterologous OsEMF1 polynucleotide. Applicant does not present a description of domains that are specific to this particular polypeptide nor domains that are important for its proper function. Given the lack of description, one skilled in the art would not be able to identify sequences with less than 100% sequence identity that still maintained the proper activity. Therefore, the written description requirement is not satisfied. Therefore, one skilled in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention. (see Written Description Requirement published in Federal Register/Vol.66, No. 4/ Friday, January 5, 2001/Notices; p. 1099-1111).

Enablement

8. Claims 1-5, 7-10, 12-16, and 18-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *In re Wands* factors (858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to an isolated nucleic acid molecule that hybridizes to SEQ ID NO:1, a sequence that hybridizes to SEQ ID NO:1 and is at least 100 nucleotides in length, or a nucleic acid sequence of SEQ ID NO:1 encoding SEQ ID NO:2, a transgenic plant and a method of modulating reproductive development in a plant, both of which comprising transforming a plant with an isolated nucleic acid molecule that hybridizes to SEQ ID NO:1 and is operably linked to a plant promoter.

Applicants isolated the rice EMBRYONIC FLOWER (EMF1) homolog, OsEMF1, from rice using the rapid amplification of cDNA ends (RACE) technique. Applicants do not disclose any of the conditions, nor primers that were used to amplify the corresponding cDNA.

Applicants have not disclosed any experiments utilizing the cloned sequence to alter the flowering time of any plant.

Applicants have not taught how one skilled in the art would use plants transformed with SEQ ID NO:1 nor have Applicants taught how one skilled in the art would use SEQ ID NO:1 to generate a specific agronomically important plant using SEQ ID NO:1 in sense orientation. Applicants have only taught the transformation of *Arabidopsis* with the *Arabidopsis* EMF1 polynucleotide encoding a polypeptide in antisense orientation. Applicants have not transformed a plant with the rice OsEMF1 polynucleotide nor have they disclosed the spatial and temporal expression needed to generate a particular phenotype. It is not clear from Applicants specification what the effect of overexpressing OsEMF1 would be on any plant phenotype.

Transforming plants with heterologous genes that are involved in plant development produce unpredictable results. Kano-Murakami et al (1993, FEBS 334:365-368) teach introducing the *Oryza sativa* homeobox 1 (OSH1) gene into tobacco. OSH1 is a rice homologue of the *Knotted-1* homeobox gene from maize and would be encompassed by Applicant's broad claim language. Kano-Murakami et al teach transgenic tobacco plants comprising the OSH1 gene display a "range of phenotypes which include abnormalities in leaf and petal shape as well as stem height and number" (page 365, right column, 1st paragraph).

The claims are broadly drawn to nucleic acid sequences that hybridize to SEQ ID NO:1 or that hybridize to SEQ ID NO:1 and are at least 100 nucleotides in length, but Applicant has not provided guidance for selecting sequences that encode a protein whose function is the same as the protein encoded by SEQ ID NO:1. The state of the art teaches isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose

contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^0C (page 859, left column, 2^{nd} paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion within the probe and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2). In the present example, the isolated fragment exhibits less than 50% sequence identity with the probe. In the present application, the selected sequences will encode proteins having modifications including additions, deletions, and substitutions of many amino acids when compared to a protein encoded by SEQ ID NO:1. Therefore, it is unpredictable as to whether any of the encoded proteins will have the same function as the protein encoded by SEQ ID NO:1.

Applicant has claimed a method of modulating reproductive development in any plant but Applicant has not even exemplified a single plant transformed with their invention and shown that it does in fact modulate development. "Modulating reproductive development" is a complex developmental process which encompasses a multitude of biological molecules that interact to culminate in a change from vegetative growth to reproductive growth. Given the complexity of the developmental process, it is unclear how one could predict that a given protein would modulate this process without first testing in some way, that it does in fact affect the process.

Applicant has not disclosed any teachings or examples in which their invention does in fact affect this process and whereby one skilled in the art could utilize the information to modulate reproductive development.

Therefore, given the unpredictability of transforming a plant with a nucleic acid involved in development to generate a particular phenotype for the reasons stated above; given the lack of guidance and examples of how one would use the isolated sequence to generate a particular phenotype; given the state of the art that teaches the unpredictability of isolating a sequence with known function using stringent hybridization conditions; given the lack of guidance and examples of isolating a sequence that hybridizes to SEQ ID NO:1 or isolating a sequence that hybridizes to SEQ ID NO:1 and is at least 100 nucleotides in length and has the same activity as SEQ ID NO:2, undue experimentation would be required by one skilled in the art to isolate a sequence encoding a protein with the same activity as the protein encoded by SEQ ID NO:1 and to use said sequence to alter flowering time in a plant.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Dorner et al (December, 1997, U.S. Patent No. 5,670,367).

Dorner et al teach a nucleic acid molecule which would hybridize under stringent conditions to SEQ ID NO:1 and is at least 100 nucleotides in length. Given that Applicant has not explicitly defined stringent conditions as noted in the 112 2nd rejection above, the Office is interpreting "stringent conditions" as any condition which facilitates hybridization of two nucleic acids.

10. No claims are allowed. SEQ ID NO:1 is deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated polynucleotide of SEQ ID NO:1.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the legal analyst, Tiffiany Tabb, whose telephone number is (703) 605-1238.

PHUONG T. BUI
PRIMARY EXAMINER 1/13/03

Stuart F. Baum Ph.D.

January 7, 2003